REMARKS

Status of the Claims

Claims 1-28 are pending in the present application. Claims 9-28 are withdrawn from consideration as directed to a non-elected invention. Claim 1 is amended for clarity. Claim 1 is further amended to specify the equation "[a]mount of plant belonging to specific plant genus (ppm (μg/g))= Fs/Ls x Lo/Fo X 1,000, 000." This equation is used in the claimed methods to quantify an amount of a plant contained in a food sample, which belongs to a specific plant genus using a correction sample copy number and a test sample copy number. Support for the equation is found throughout the application as originally filed including, *e.g.*, on page 21, lines 15-16 and page 59, lines 5-20. Further support is found on page 24, lines 2-7, which states "[f]or preparing the sample for correction and the test sample, it is preferred that the sample derived from the specific plant genus in the sample for correction and the sample of the food or the food ingredient in the test sample should be used in almost the same amounts, and that the standard plant sample in the sample for correction and the sample derived from the standard sample in the test sample should be used in almost the same amounts."

Based upon the foregoing, the present application supports the amendments to claim 1. Accordingly, no new matter is entered. Reconsideration is respectfully requested.

Objection to the Specification

The specification is objected to for containing hyperlinks. Embedded hyperlinks have been deleted. Accordingly, Applicants respectfully request withdrawal of the objection.

Issues Under 35 U.S.C. § 102(b)

Claims 1-3 and 6 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Terry *et al.*, *European Food Research and Technology*, 2001, 213:425-431, ("Terry"). For the reasons set forth below, Applicants respectfully traverse.

As amended, claim 1 is directed to a method of quantifying a plant belonging to a specific plant genus in a food or a food ingredient by a PCR method, comprising: preparing a sample for correction where a sample derived from the specific plant genus to be detected and a

standard plant sample are mixed in a predetermined ratio, and extracting genomic DNA from the sample for correction; preparing a test sample where a food or the food ingredient to be examined and a standard plant sample are mixed in the same amount as the above sample for correction, and extracting genomic DNA from the test sample; practicing a quantitative PCR using a primer set for detecting the sample derived from the specific plant genus to be detected and a primer set for detecting the standard plant sample with the genomic DNA extracted from each of the sample for correction and the test sample as a template; determining the copy number of the DNA derived from the standard plant (Lo) and the copy number of the DNA derived from the specific plant genus (Fo) for the sample for correction by the quantitative PCR method; and determining the copy number of the DNA derived from the specific plant genus (Fs) and the copy number of the DNA derived from the standard plant (Ls) for the test sample by the quantitative PCR method, and calculating the amount of the plant belonging to the specific plant genus contained in the food or the food ingredient using the above copy numbers according to the following equation: Amount of plant belonging to specific plant genus (ppm (μg/g)) = Fs / Ls x Lo / Fo x 1,000,000.

Based upon the foregoing, claim 1 describes a method, which comprises simultaneously extracting DNA derived from a specific plant genus, which is to be detected, and DNA derived from a standard plant, which is from two prepared samples, *i.e.* a correction sample and a test sample; each of the samples is externally supplemented with a standard plant sample. DNA copy number of each of these plant types is determined using the quantitative PCR method. This novel, non-obvious method is highly reliable and quantification can be accurately achieved, given that any variation due to, *e.g.*, DNA extraction efficiency or PCR inhibition is controlled, since such variation, which may affect the specific plant genus, which is to be detected, will also affect the standard plant in the samples.

In contrast to the instant claims, Terry describes a technique for detection of genetically modified crops, *e.g.*, soybean, using a conventional quantitative PCR method. Terry further teaches that an endogenous gene, *e.g.*, lectin is used as the standard, *see e.g.*, page 426, Table 1.

Terry fails to teach all of the elements of the instant claims. In fact, Terry and the instant claims do not share any common technical features.

In contrast to the instantly claimed methods, Terry describes a method for detection of genetically modified crops (soybean) using a conventional quantitative PCR method. The instant application distinguishes conventional quantitative PCR methods from the instant invention, *see e.g.*, Background, page 3, lines 16-27. As described in the instant application, such conventional PCR methods as described in Terry, are useful for detecting recombinant crops among the same crop species, *e.g.*, genetically modified soybeans among soybeans, or genetically modified corn among corn. Conventional quantitative PCR methods are further characterized in that any correction for PCR variation, *e.g.*, inhibition of PCR reactions, is not accomplished by externally adding a plant or purified DNA from a plant as a standard, such as specified in the instant claims. Instead, the conventional quantitative PCR methods of Terry use an endogenous gene, *e.g.*, lectin, as a standard, which is specific to the plant that is to be detected.

The instant methods do not specify the use of conventional quantitative PCR using endogenous genes as a standard, which are specific to the plant being detected. Instead, **the instant claims describe a method wherein DNA is simultaneously extracted from a specific plant genus, which is to be detected, and DNA derived from a standard plant, which is from two prepared samples, *i.e.*, a sample for correction and a test sample. These samples are each externally supplemented with the standard plant sample. Accordingly, the claimed method does not use endogenous genes, which are specific to the plant to be detected, as standards.** Standard plants encompassed by the instant claims include, *e.g.*, statice, *Limonium*. Quantitative PCR is then used to detect and quantify the plant genus of interest, *see also* page 8, lines 15-23 in the presently filed application.

Accordingly, the correction methods used in Terry are completely distinguishable from the correction steps described in the claimed methods. That is, Terry uses an endogenous gene as a standard and the instantly claimed methods describe "DNA of a standard plant externally added."

As noted above, conventional PCR methods, such as those described in Terry, are suitable for quantifying the content of recombinant plants in a sample, which consists of the same plant species, such as a sample consisting of only soybean species. Conventional PCR methods are suitable for such use because an endogenous gene can be selected for use as an

internal standard, which has a nucleotide sequence that is universal to the cultivars within a species. Accordingly, the copy number obtained from an endogenous gene will generally be the same across the cultivar varieties. However, an endogenous gene would not be appropriate for use as an internal standard for detecting a quantity of an allergenic-specific ingredient present in a mixture, which consists of various living species components, as well as inanimate components. This is due to the fact that it is difficult to find an endogenous sequence, for use as an internal standard, which is common to DNAs from a variety of living species. *See e.g.*, page 3, line 2 from the bottom to page 4, line 8. Accordingly, conventional quantitative PCR methods are not useful for such purposes.

The presently claimed methods allows for quantitative detection of a specific food contaminant or a contaminant of a food ingredient, with greater accuracy, specificity and sensitivity. The instantly claimed methods are also highly reproducible, highly reliable and allow the reliable exclusion of false positives.

Based upon the foregoing, claim 1 is not anticipated by Terry. Further, claims 2, 3, and 6, which incorporate the elements of independent claim 1, also are not anticipated by the cited reference. Accordingly, Applicants respectfully request withdrawal of the rejection.

Issues Under 35 U.S.C. § 103(a)

Claim 8

Terry and Hirao

Claim 8 is rejected under 35 U.S.C. § 103(a) as allegedly obvious over Terry in view of U.S. Publication No. 2003/0207298 to Hirao et al., ("Hirao"). Applicants respectfully traverse.

Claim 8, which incorporates the elements of independent claim 1, specifies that the plant genus to be detected is the genus *Fagopyrum*, a primer set for detecting the genus *Fagopyrum* is a set consisting of an oligonucleotide having a sequence shown in SEQ ID NO: 14 and an oligonucleotide having a sequence shown in SEQ ID NO: 15, and a probe for detecting the genus *Fagopyrum* is an oligonucleotide having a sequence shown in SEQ ID NO: 64.

As noted above, Terry fails to teach the method described in claim 1. That is, claim 1 is so utterly different from the methods described in Terry that there are no common technical features between them.

Hirio fails to remedy the deficiencies of Terry. Hirio describes a method for detecting a target plant genus, including *Fagopyrum*, by PCR, using primers having a design that is based upon the rDNA Internal Transcribed Spacer (ITS)-1 or ITS-2 sequences of the target plant genus. Hirao teaches the primers described in instant claim 8. However, Hirao fails to teach or suggest the probe described in the instant claim. Although Hirao teaches the application of PCR-based methods, Hirao does not teach or suggest the specific steps as defined in claim 1. In addition, Hirao fails to teach or suggest correcting any errors due to PCR or variation in DNA extraction by using external DNA as a standard.

Further, the methods of the present invention result in unexpected benefits. The claimed methods may be used for quantitative detection of specific components, which contaminate a food or a food ingredient. The claimed methods may be used with greater accuracy, high specificity and sensitivity. Further, the claimed methods are highly reproducible, the measurements are reliable, and false positives can be reliable excluded. Such remarkable, unexpected effects were only achieved by the instantly claimed methods, and cannot be attained by any conventional methods, including the method described by Terry in view of Hirao.

Based upon the foregoing, claim 8 is not obvious over Terry in view of Hirao. Accordingly, Applicants respectfully request withdrawal.

Claims 4 and 5

Claims 4 and 5 are rejected as allegedly obvious over Terry in view of Palacios *et al.*, *Molecular Phylogenetics and Evolution*, 2000, 14:232-249, ("Palacios"), *see* Office Action, pages 7-8. Based upon the following, Applicants respectfully traverse.

Claim 4, which incorporates the elements of claim 1, specifies that the standard plant belongs to a plant species other than upland weeds and food crops. Claim 5, which also incorporates the claim 1 elements, specifies that the standard plant is statice.

As noted previously, Terry fails to teach the method described in claim 1. Palacios fails to remedy Terry's deficiencies.

The Palacios reference describes an evolutionary relationship study among statice varieties using ITS sequences. The Palacios reference discloses oligonucleotides used as primers for amplification of the statice rDNA ITS region sequences. The disclosed primers are universal eukaryotic primers. Such primers were originally designed for analysis of the rDNA region of eukaryotes, such as fungi. Accordingly, the disclosed oligonucleotides can amplify not only the rDNA ITS region from statice, but also from various other plant, fungi or the like. Accordingly, the oligonucleotides described in the Palacios reference cannot be effectively used to detect allergens in food using quantitative PCR.

In addition, the Palacios reference does not teach or suggest the method steps specified in claim 1, statice as the standard plant, as specified in claim 5 or the unexpected advantages of the claimed methods described above. Based upon the foregoing, Applicants submit that claims 4 and 5 are not obvious over Terry in view of Palacios. Accordingly, Applicants respectfully request withdrawal of the rejection.

Claim 7

Claim 7 is rejected under 35 U.S.C. § 103(a) as allegedly obvious over Terry in view of Palacios and further in view of GenBank Accession No. AJ222860, and further in view of Buck *et al.*, *BioTechniques*, 1999, 27:528-536, ("Buck"). Applicants respectfully traverse.

Claim 7, which incorporates the elements of claim 1, specifies that the standard plant is statice, a primer set for detecting the statice is a set consisting of an oligonucleotide having a sequence shown in SEQ ID NO: 57 and an oligonucleotide having a sequence shown in SEQ ID NO: 58, and a probe for detecting the statice is an oligonucleotide having a sequence shown in SEQ ID NO: 59.

As noted above, Terry does not teach the elements of independent claim 1. Also, as noted above, Palacios does not remedy the deficiencies of Terry. GenBank Accession Number AJ222860 and Buck also fail to remedy the deficiencies of Terry and Palacios. GenBank Accession Number AJ222860 merely discloses the statice 18S rRNA, 26S rRNA, ITS-1 and ITS-2 sequences. Buck is merely cited for disclosing an analysis of the effect of a primer design strategy on the performance of DNA sequence primers, *see* Office Action, page 9. Further the

advantages of the claimed method, as described above, would not have been expected from the cited references. Accordingly, none of the references, either alone or in combination, teach or suggest all of the elements of the instant claims or render the instant claim obvious. Based upon the foregoing, Applicants respectfully request withdrawal of the rejection.

Claim 8

Terry, Nair, Yasui and Buck

Claim 8 is rejected under 35 U.S.C. § 103(a) as allegedly obvious over Terry in view of Nair *et al.*, *Fagopyrum*, 1999, 16:29-36, ("Nair") and further in view of Yasui *et al.*, *Genes and Genetic Systems*, 1998, 73:201-210, ("Yasui") and further in view of Buck. Applicants respectfully traverse.

As note above, Terry fails to teach or suggest all of the elements of independent claim 1. Nair merely demonstrates that *Fagopyrum* (buckwheat) is an allergenic protein, which can be detected by the PCR method. Yasui merely shows that a DNA sequence, of about 0.7kbp, which includes ITS-1 region sequences, ITS-2 regions sequences and the 5.8S rRNA gene, shown in Figure 2 of Yasui, may be used to analyze the lineage of the *Fagopyrum* genus. As noted above, Buck merely discloses an analysis of the effect of a primer design strategy on the performance of DNA sequence primers and generally referred primer designs. Further the advantages of the claimed methods, as described herein, would not have been expected from the cited references. Accordingly, Nair, Yasui or Buck, neither alone nor in combination, remedy the deficiencies of Terry.

Based upon the foregoing, the claims are not obvious over the cited references and Applicants respectfully request withdrawal of the rejection.

CONCLUSION

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Linda T. Parker, Ph.D., Reg. No. 46,046, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

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